

**REMARKS**

Applicants thank the Examiner for discussions regarding the pending Application during the week of February 10, 2003. Applicants also remind the Examiner about plans to consult with Applicants about the pending Application after receipt of this Amendment and Request of Continued Examination.

Claims 1-18 and 23-26 are pending this the Application. Pending claims are rejected in the Advisory Action as stated:

Continuation of 5 does NOT place the application in condition for allowance because: applicant's arguments were not found to be persuasive. Specifically, Applicant argues that Cleland teaches limitations which are not required by Applicant's invention. This argument is not found to be persuasive because Applicant's claims incorporate "comprising" language, and therefore, do not exclude additional steps from being presented in a reference. (Emphasis in original)

In the Claims, please amend claims 1, 23, and 24. Claims 2-18 and claims 25-36 remain in the Application as depending from Amended claims 1, 23, and 24. Applicants believe claims 1, 23, and 24 as Amended are now drawn to a novel invention with steps excluded by cited prior art references, specifically the limitation "and wherein no additional emulsification is performed." As such, Applicants respectfully request the rejection of Amended claims 1, 23, and 24 be withdrawn. Similarly, Applicants respectfully request the rejection of claims 2-18 and 25-36 be withdrawn, as these claims properly depend from Amended claims now drawn to a novel invention.

Support for the Amendment to claims 1, 23, and 24 can be found throughout the Specification with some specific examples shown below.

The double-emulsion technique is the most commonly reported method for manufacturing microspheres. According to this technique, protein dissolved in an aqueous solution is then emulsified in an organic solvent containing the dissolved PLGA. The aqueous-organic emulsion is then further emulsified in an aqueous alcohol phase to create an aqueous-organic-aqueous double emulsion. The alcohol phase extracts the organic solvent away from the PLGA in approximately one hour, leaving the protein entrapped in discrete droplets within solid microspheres. The process of emulsifying the aqueous protein solution in the organic solvent, however, can easily denature the protein. (Page 3, ll. 22-24 through page 4, ll. 1-9; emphasis added)

The present invention solves the problems in the prior art just described by providing a solid-encapsulation/single-emulsion/ solvent extraction technique to encapsulate solid proteins and other bioactive substances into biodegradable microspheres. (Page 7, ll. 3-7; emphasis added).

**CONCLUSION**

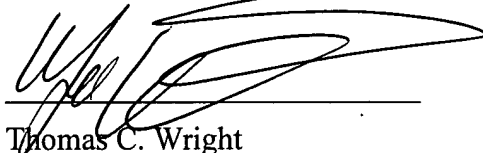
This Amendment is being filed concurrently with Request for Continued Examination (RCE) Transmittal. The Amendment does not add new matter and does not reflect a departure therefrom in substance or variation in the disclosure from application Serial No. 09/671,540, filed September 27, 2000.

This Amendment does not increase the number of claims. If, however, our calculations are in error and a fee is due, please charge this fee to Deposit Account No. 07-0153. Please feel free to telephone the undersigned at the phone number listed below if there are any questions.

Dated: February 18, 2003

Respectfully submitted,

GARDERE WYNNE SEWELL LLP

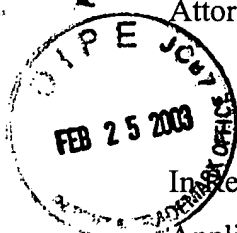
A handwritten signature in black ink, appearing to read 'Thomas C. Wright', is written over a horizontal line.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Inventor: Timothy W. King and Charles W. Patrick  
 Application Serial No.: 09/671,540  
 Group Art Unit: 1615  
 Examiner: Amy E. Pulliam  
 Date Filed: September 27, 2000  
 Title: COMPOSITIONS AND METHODS FOR  
 BIODEGRADABLE MICROSPHERES AS CARRIERS OF  
 BIOACTIVE SUBSTANCES

MARKED-UP COPY OF AMENDED CLAIMS  
 IN ACCORDANCE WITH C.F.R. § 1.121

1. (AMENDED, VERSION 1) A method for making microspheres comprising a bioactive substance, the method comprising:

dissolving a polymer with an organic solvent to produce a polymer solution;

adding a biologically effective amount of a bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance;

vibrating the mixture to produce a bioactive substance-polymer complex;

emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and

extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the bioactivity of the bioactive substance is usefully preserved and wherein no additional emulsification is performed.

23. (AMENDED) A method for making microspheres comprising a solid bioactive substance, the method comprising:

dissolving a polymer with an organic solvent to produce a polymer solution;

adding a biologically effective amount of a solid bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance;

vibrating the mixture to produce a bioactive substance-polymer complex;  
emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and  
extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the bioactivity of the bioactive substance is usefully preserved and wherein no additional emulsification is performed.

24. (AMENDED) A method for microencapsulating a bioactive substance, the method comprising:

providing a bioactive substance;  
providing at least one polymer;  
providing an organic solvent;  
dissolving the polymer in a volume of the organic solvent to produce a polymer solution;  
adding the bioactive substance to the solution to produce a mixture of the polymer and the bioactive substance;  
vibrating the mixture to produce a bioactive substance-polymer complex;  
emulsifying the mixture to produce an emulsion comprising the bioactive substance-polymer complex; and  
extracting the organic solvent from the emulsion to produce microspheres comprising the polymer-bioactive substance complex, wherein the biological activity of the bioactive substance is substantially preserved and wherein no additional emulsification is performed.